LETTER TO THE EDITOR

Neurofibromatosis: No Chromosomal Defect by Prophase Banding Technique

Von Recklinghausen's neurofibromatosis (NF) is a genetic disorder with a broad range of severity and manifestations, including neoplasia and birth defects [1]. Although considered an autosomal dominant trait, its genetics may be heterogeneous, since NF has the highest mutation rate of any human locus, and 50% of patients represent new sporadic occurrences. High resolution karyotyping has provided insights into the genetics of other syndromes of cancer and congenital malformations, e.g., aniridia-growth retardation with Wilms' tumor and growth and mental retardation with retinoblastoma [2]. Hence, we studied NF cells with our new simple prophase technique [3].

Through the local chapter of the National Neurofibromatosis Foundation, volunteers were recruited who had at least two of the following features: (a) six or more café-au-lait spots at least 1.5 cm in greatest diameter (or, if under 10-years-of-age, two or more spots at least 0.5 cm); (b) biopsy-proved NF; (c) a skin nodule consistent with neurofibroma; (d) a major, rare manifestation of NF (one patient each had optic nerve glioma, lateral meningocoele, tibial pseudarthrosis, and macrodactyly); and (e) a first-degree relative meeting the above criteria. The ten female and four male subjects from nine families were 3–46 years old (median, 23) and had no acute illnesses. One had received radiotherapy for breast cancer.

After informed consent, blood was drawn and processed [3]. Phytohemagglutinin-stimulated lymphocytes were incubated for 72 hr followed by treatment of the cells for 10 min with 10 ml hypotonic solution consisting of equal parts of 75 mmol/L 2-mercaptoethanol and 75 mmol/L KCl. Then, 0.5 μg of colcemid were added and the cells incubated for an additional 10 min. The incubation was ended by fixing the cell suspension with several changes of a 3:1 mixture of absolute methanol and glacial acetic acid. Slides were prepared and aged in the usual manner, then subjected to trypsin-Giemsa staining. For each individual, at least 10 prophases were completely karyotyped and 15 more were partially karyotyped.

There was no chromosomal anomaly seen in any individual. If a chromosomal defect occurs in some patients with NF, it likely affects fewer than 640–720 kb, the resolution typically achieved by our 1000-band technique. To suggest a chromosomal localization of the NF gene(s), techniques more powerful (albeit, more arduous) than karyotyping must be applied; indeed, genetic linkage analysis with 28 conventional markers recently suggested a locus on chromosome #4, near GC, a serum protein [4]. Additional families should be studied, perhaps adding, as markers, the polymorphisms of DNA restriction fragment lengths that were so successful in assigning the gene locus for Huntington's disease to chromosome #4 [5].

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